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10/684,633	10/14/2003	Michael S. Kopreski	00-1312-L	5239

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McDonnell Boehnen Hulbert & Berghoff
32nd Floor
300 S. Wacker Drive
Chicago, IL 60606

EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,633	KOPRESKI, MICHAEL S.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-11,13,14 and 16-35* is/are pending in the application.

4a) Of the above claim(s) *1,3,5-11,13,14 and 16-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IC in the reply filed on December 17, 2008 is acknowledged. The traversal is on the ground(s) that "[A]pplicant traverses this ground of rejection on two grounds. First, the Action does not establish or provide any support for the statement that Applicant's claims satisfy any of the criteria listed on pp. 4-5 of the Action. Second, the assertions in the Action that there would be an undue burden on the Office in searching all of the claims pending at the time of this Action is unsupported by the classification determinations contained in the Action. All of the claims are categorized by the Action itself as falling within class 435, subclass 91; that claims grouped in Group IB may contain unspecified subject matter falling in subclass 91.1 rather than 91.2 is not compelling evidence of an undue burden. Applicant also traverses on the grounds that prosecution of the claims pending at the time the current Action was issued was sufficiently advanced that imposing a restriction requirement would be contrary to the goal of both Applicant and the Office to promote efficient and expeditious examination. Applicant respectfully contends that while there may be instances where amendments or the course of prosecution mandate restriction (instead of an election of species, for example) to expedite prosecution, this is not one of them".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that Groups IA to IC will be examined together. First, since, as shown in pages 3 and 4 of the restriction requirement mailed on November 17, 2008, the searches for Groups IA to IC are different, applicant's argument "the Action does not establish or provide any support for the

statement that Applicant's claims satisfy any of the criteria listed on pp. 4-5 of the Action" is incorrect. Second, the restriction is not based on different classifications and "imposing a restriction requirement would be contrary to the goal of both Applicant and the Office to promote efficient and expeditious examination" as argued by applicant. Third, although applicant has amended claims 33-35 in Group IC, since Groups IA and IB require to search a specific cancer while amended claims 33-35 in Group IC does not require to search a specific cancer, the searches for Groups IA IB, and IC are different. The requirement is still deemed proper and is therefore made FINAL. Claims 33-35 will be examined.

2. This application contains claims 1, 3, 5-11, 13,14 and 16-32 drawn to an invention nonelected with traverse in the reply filed on September 28, 2006 and December 17, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Scope of Enablement

Claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting a tumor-associated heterogeneous nuclear ribonucleoprotein RNA A2/B1 in blood plasma and serum, and pleural fluid from a specific human, does not reasonably provide enablement for detecting any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma and serum, and pleural fluid from a human as

recited in claims 33-35. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method for detecting a tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma from a human, a method for detecting a tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in serum from a human, and a method for detecting a tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in pleural fluid from a human. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.,* 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claim 33 is directed to a method for detecting any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma of a human. Claim 34 is directed to a method for detecting any kind of tumor-associated heterogeneous nuclear

ribonucleoprotein RNA species in serum from a human. Claim 35 is directed to a method for detecting any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in pleural fluid from a human.

Working Examples

The specification provides working examples for: (1) detecting her-2/neu RNA in blood plasma of a 44 year old woman who is diagnosed with metastatic breast cancer; (2) detecting EGFR RNA in blood serum of a 56 year old man who is diagnosed with colorectal cancer; and (3) detecting her-2/neu RNA, hnRNP A2/B1 RNA and hTERT RNA in pleural fluid of a 60 year old man who is diagnosed with lung cancer (see pages 25-26). The specification provides no working example for detecting any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35.

The Amount of Direction or Guidance Provided and The State of The Prior Art

Although the specification provides a guidance for detecting hnRNP A2/B1 RNA in blood plasma and blood serum (see pages 3-10), and in pleural fluid of a 60 year old man who is diagnosed with lung cancer (see pages 25-26), the specification does not provide a guidance for detecting any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention. Although it is known in the art that heterogeneous nuclear ribonucleoprotein

RNA B1 (HnRNP B1) mRNA can be detected in blood serum and plasma of lung cancer patients (see Fleischhacker et al., Annals of The New York Academy of Sciences, 945, 179-188, 2001 and Sueoka et al., Lung Cancer, 48, 77-83, 2005), during the process of the prior art search, the examiner has not found any prior art which is related to detect any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species can be detected in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35. First, although the specification provides a guidance for detecting hnRNP A2/B1 RNA in blood plasma and blood serum (see pages 3-10), and in pleural fluid of a 60 year old man who is diagnosed with lung cancer (see pages 25-26), and it is known in the art that heterogeneous nuclear ribonucleoprotein RNA B1 (HnRNP B1) mRNA can be detected in blood serum and plasma of lung cancer patients (see Fleischhacker et al., Annals of The New York Academy of Sciences, 945, 179-188, 2001 and Sueoka et al., Lung Cancer, 48, 77-83, 2005), tumor-associated heterogeneous nuclear ribonucleoprotein RNA includes HnRNP A1, HnRNP A2/B1, HnRNP A2/B2, HnRNP B1, HnRNP C1/C2, HnRNP E1, HnRNP F, HnRNP H, HnRNP H/H', HnRNP I, HnRNP K, and HnRNP M4 which can expressed in different types of cancers (see Table 2 in page 95 from Carpenter et al., Biochimica

et Biophysica Acta, 1765, 85-100, 2006), tumor-associated heterogeneous nuclear ribonucleoprotein RNA recited in claims 33-35 is not limited to HnRNP A2/B1 RNA and HnRNP B1 RNA and the specification does not provide a guidance to show any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species such as HnRNP A1, HnRNP A2/B2, HnRNP C1/C2, HnRNP E1, HnRNP F, HnRNP H, HnRNP H/H', HnRNP I, HnRNP K, and HnRNP M4 can be detected in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35. Thus, it is unclear whether any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species such as HnRNP A1, HnRNP A2/B2, HnRNP C1/C2, HnRNP E1, HnRNP F, HnRNP H, HnRNP H/H', HnRNP I, HnRNP K, and HnRNP M4 can enter blood plasma and serum, and pleural fluid so that any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species such as HnRNP A1, HnRNP A2/B2, HnRNP C1/C2, HnRNP E1, HnRNP F, HnRNP H, HnRNP H/H', HnRNP I, HnRNP K, and HnRNP M4 can be detected in blood plasma and serum, and pleural fluid. Second, since claims 33-35 do not limit human to a specific human, since it is known that positivity of hnRNP B1 mRNA in plasma is 12% for healthy volunteers, 20.8% for benign lung diseases, 57.1% for non-lung cancer neoplasm, and 45.5% for lung cancer patients (see page 80, left column from Sueoka et al., Lung Cancer, 48, 77-83, 2005), it is unclear why a fraction of extracted RNA from plasma or serum from any kind of human can comprise a tumor-associated heterogeneous nuclear ribonucleoprotein RNA species such as hnRNP B1 mRNA as recited in step b) of claim 33 and step a) of claim 34. In view of above discussions, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether

any kind of tumor-associated heterogeneous nuclear ribonucleoprotein RNA species can be detected in blood plasma and serum, and pleural fluid from a human as recited in claims 33-35.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working example related to the claimed invention recited in claims 33-35 and the no teaching in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 33 is rejected as vague and indefinite in view of step c) because it is unclear what kind of signal produced using labeled primers or probes specific for tumor-associated heterogeneous ribonucleoprotein RNA species, or cDNA therefrom can be considered as an amplified signal. Please clarify.

8. Claims 34 and 35 are rejected as vague and indefinite in view of step b) because it is unclear what kind of signal produced using labeled primers or probes specific for tumor-associated heterogeneous ribonucleoprotein RNA species, or cDNA therefrom can be considered as an amplified signal. Please clarify.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Frank W Lu /
Primary Examiner, Art Unit 1634
February 26, 2009